UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/987,687	11/15/2001	Matthew C. Coffey	032775-078	7186

7590 02/26/2003

Gerald F. Swiss
BURNS, DOANE, SWECKER & MATHIS, L.L.P.
P.O. Box 1404
Alexandria, VA 22313-1404

EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	14

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/987,687	COFFEY ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1 136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/12/02 has been entered.

2. This Action is in response to the communication filed on 12/12/02, as Paper No. 13. Claims 1-20 are pending in the application and are examined herein. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 7 and 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Kooby et al. (FASEB Journal, Aug. 1999; 13:1325-1334).

Kooby teaches a method for delivering a virus to a solid tumor to reduce growth of the tumor, comprising administering an effective amount of virus to a subject bearing the tumor, wherein the virus is capable of selectively replicating in and killing tumor cells, by a base administration selected from the group consisting of:

(a) delivering a composition comprising the virus to multiple sites inside the tumor; and

(b) delivering directly into the tumor a composition comprising the virus, wherein the volume of the viral composition is between about 10% and 100% of the volume of the tumor

Kooby also teaches that the virus is a modified herpes simplex virus (HSV) and that the virus is delivered to one site per 0.25 cm^3 of the tumor, wherein the total volume of the virus composition is at least 30%, at least 50% or between about 10% to about 100% of the volume of the tumor.

Specifically, Kooby teaches that multi-mutated HSV type-1 virus (G207) is a replication-competent HSV type-1 (HSV-1) which has demonstrated impressive oncolytic activity in several neurological malignancies, while sparing normal neural tissue (see paragraph bridging p. 1325-1326). Kooby indicates that human colorectal cancer cells were injected into athymic rats and allowed to grow until the tumor volume reached ~50mm^3, the tumors were then injected with 50µl of a G207 viral composition (See p. 1327, first full paragraph). It is noted that ~50mm^3= ~0.050ml= ~50µl. Therefore, injecting 50µl constitutes injecting about 100% of the volume of the tumor (which is at least 30%, at least 50% and in the range of about 10% to about 100% of the volume of the tumor). Kooby teaches that direct injection of the virus composition suppressed xenograft tumor growth significantly compared to controls (see p. 1328, last full

paragraph; and p. 1330, Figure 4). Furthermore, Kooby teaches a single injection of the virus composition to a tumor that has a volume= ~50mm^3, thus meeting the limitation of claim 10, wherein the virus is delivered to one site per about 0.25 cubic centimeters of the tumor. It is noted that 0.25cm^3 = 250mm^3, thus a tumor with a volume of 50mm^3 would only require a single injection.

It is noted that claim 1 limits the method of delivery to either (a) delivering a composition comprising the virus to multiple sites inside the tumor, or (b) delivering directly into the tumor a composition comprising the virus, wherein the volume of the viral composition is between about 10% and 100% of the volume of the tumor. Kooby teaches administering a viral composition that is about 100% of the tumor volume, clearly meeting the limitation of claim 1(b). Furthermore, claim 1(a) indicates that the administration must deliver the composition comprising the virus to multiple sites inside the tumor. Looking to the specification for guidance on the definition of "multiple sites inside the tumor" it is noted that the specification does not explicitly define "multiple sites inside the tumor", but does indicate, "Alternatively, the virus can be delivered to a single site in a large amount of fluid, which enables a wider spread of the virus" (See p. 14, lines 5-10 of the instant specification). Therefore, claim 1(a) can be interpreted to encompass delivering a single injection of a large volume of the virus (about 100% of the volume of the tumor is considered to be a large volume) to a tumor resulting in the viral composition spreading to other sites (i.e. cells) inside the tumor. Kooby also teaches a method which meets this interpretation of claim 1(a).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-6 and 14-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kooby et al. (FASEB Journal, Aug. 1999; 13:1325-1334) in view of Lee et al. (WO 99/08692 filed 12 August 1998 and published on 25 February 1999).

Kooby teaches a method for delivering a virus to a solid tumor to reduce growth of the tumor, comprising administering an effective amount of virus to a subject bearing the tumor, wherein the virus is capable of selectively replicating in and killing tumor cells, by a base administration selected from the group consisting of:

(a) delivering a composition comprising the virus to multiple sites inside the tumor; and

(b) delivering directly into the tumor a composition comprising the virus, wherein the volume of the viral composition is between about 10% and 100% of the volume of the tumor, as indicated in the rejection of claim 1 above.

Kooby does not teach that the virus can be a reovirus, a mammalian reovirus, a human reovirus, a serotype 3 human reovirus, or a Dearing strain serotype 3 human reovirus or that the method of delivery further comprises at least one additional administration delivering a composition comprising the virus to multiple sites inside the solid tumor (see claim 14 (a)) or additionally delivering directly into the tumor a composition comprising the virus, wherein the volume of the virus composition is between about 10% and about 100% of the volume of the tumor (see claim 14(b)).

However, Lee teaches a method for delivering a reovirus serotype 3 Daring strain virus to a solid tumor to reduce growth of the tumor, comprising administering an effective amount of virus to a subject bearing the tumor, wherein the virus is capable of selectively replicating in and killing tumor cells and wherein the virus is administered in a single dose or in multiple doses (i.e. more than one does) and the multiple doses can be administered concurrently (at the same time) or consecutively (i.e. either before or after the base administration). (See, for instance, abstract; p.3 lines 1-15; p.9, lines 17-20; p.34, lines 9-17; Examples 9 and 10; and Claim 38). Lee also teaches that the reovirus is not known to be associated with disease (see p. 3, lines 15-18), thus making it a safer therapeutic virus than viruses that are known to cause diseases.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by Kooby such that the viral vector that is delivered into the tumor is a Dearing strain serotype 3 virus, and to modify the method of

Lee such that the method comprises either an additional administration of the virus composition to multiple sites inside the tumor (either concurrently or before or after the base administration) or an additional direct injection of the virus composition wherein the virus composition comprises a volume between about 10% to about 100% of the volume of the tumor, with a reasonable expectation of success.

One of ordinary skill would have been motivated to substitute the modified HSV-1 virus of Kooby with the Dearing strain 3 reovirus of Lee in order to increase the safety of the method as herpes viruses are known to causes diseases in subjects while reovirus is not known to be associated with any disease. Furthermore, one of ordinary skill would have been motivated to modify the method of Kooby such that the method further comprises an additional administration of the virus composition to the tumor wherein the composition is either administered to multiple sites inside the tumor (either concurrently or before or after the base administration) or another injection of the composition comprising a volume between about 10% to about 100% of the volume of the tumor is administered to the tumor in order to sufficiently treat the tumor because Lee indicates that effective treatment depends on several factors including the amount of virus administered, the type and size of the tumors and indicates that multiple doses may be required (see p. 9, lines 7-20).

8. Claims 1, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kooby et al. (FASEB Journal, Aug. 1999; 13:1325-1334) in view Barber et al. (US Patent 5,662,896, published 1997).

Kooby teaches a method for delivering a virus to a solid tumor to reduce growth of the tumor, comprising administering an effective amount of virus to a subject bearing the tumor, wherein the virus is capable of selectively replicating in and killing tumor cells, by a base administration selected from the group consisting of:

(a) delivering a composition comprising the virus to multiple sites inside the tumor; and

(b) delivering directly into the tumor a composition comprising the virus, wherein the volume of the viral composition is between about 10% and 100% of the volume of the tumor, as indicated in the rejection of claim 1 above.

Kooby does not teach that the virus is delivered to at least 3 (claim 8) or at least 5 sites (claim 9) inside the tumor mass.

However, Barber teaches a method for delivering a virus which kills tumor cells (and may be a non-pathogenic, replication competent virus (see col. 10, lines 64-65)) to multiple sites within the mass of the tumor. Specifically, Barber teaches, "Various methods may be utilized within the context of the present invention in order to directly administer the vector construct to the tumor." "For example, within one embodiment a small metastatic lesion may be located and the vector injected several times in several different locations within the body of the tumor" (emphasis added, see col. 11, lines 5-8), thus indicating administration of at least 3 injections (because "several" indicates "greater than two but less than many", as defined in Merriam-Webster's Collegiate Dictionary, Tenth Edition, pg. 1073 as mentioned in the previous Office Action).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to modify the method of Kooby such that the method comprised delivering the virus to several

different sites (such as at least 3, at least 5, or more sites) inside the tumor mass in order to effectively treat the tumor. The exact number of times would be a matter of routine experimentation in order to determine the most effective number of sites to deliver the virus.

One of ordinary skill would have been motivated to combine the references in order to more effectively treat the tumor because Barber teaches a method comprising administering a replication competent virus to several different sites inside a tumor in order to treat the tumor. Specifically, Barber teaches a working example wherein multiple injections of the virus are given to the tumor every two to three days (see col. 37, lines 44-45), thus indicating administering multiple injections on day zero and then more multiple injections on either day 2 or day 3 in order to treat a tumor in a subject.

Response to Arguments

The rejection of claims under 35 USC 102 and the rejection of claims under 35 USC 103 are withdrawn as Barber does not explicitly indicate that the virus used in the method selectively replicates in the tumor cells, only that the virus is replication competent and can kill tumor cells.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell
February 21, 2003

DAVE T. NGUYEN
PRIMARY EXAMINER